



## **Severe Acute Respiratory Syndrome (SARS) February 2005**

1: Am J Respir Crit Care Med. 2005 Jan 18; [Epub ahead of print]

Characterization of Cytokine and Chemokine Profiles of Severe Acute Respiratory Syndrome.

Jiang Y, Xu J, Zhou C, Wu Z, Zhong S, Liu J, Luo W, Chen T, Qin Q, Deng P.

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**Rationale:** There is currently no optimal treatment or effective drug for severe acute respiratory syndrome (SARS) due to a poor understanding of the immunopathological mechanism. **Objectives:** To explore the immune mechanism underlying the pathogenesis of SARS, we studied the expression profile of cytokines/chemokines in the blood and the immunopathology of the lung and lymphoid tissues. **Methods:** Fourteen cytokines/chemokines in the blood of 23 SARS patients were dynamically screened using a bead-based multi-assay system. Reverse-transcription PCR was performed for amplifying the messenger RNA. Histopathology of the lung and lymphoid tissues of autopsy was examined using methods of immunohistochemistry and double immunofluorescent staining. **Main Results:** Interferon-inducible protein 10 (IP-10) elevated markedly in the blood at the early stage of SARS, and maintained a high level until convalescence. Moreover, IP-10 was highly expressed in both lung and lymphoid tissues where monocyte/macrophage infiltration and depletion of lymphocytes were observed. The levels of interleukin 6 (IL-6), interleukin 8 (IL-8) and monocyte chemoattractant protein 1 (MCP-1) were concomitantly increased in the blood of the patients with superinfection, and the mRNAs for these cytokines were also increased in the lung tissues. **Conclusions:** Induction of IP-10 is a critical event in the initiation of immune-mediated acute lung injury and lymphocyte apoptosis during the development of SARS. Superinfection following the immune injury is the main cause of death. The prompt elevation of IL-6, IL-8 and MCP1 is a sign of superinfection indicating a high risk of death.

PMID: 15657466 [PubMed - as supplied by publisher]

2: Ann Intern Med. 2005 Feb 1;142(3):225; author reply 225-6.

Comment on:

Ann Intern Med. 2004 Sep 7;141(5):333-42.

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Veterans Health Administration

A clinical prediction rule for the severe acute respiratory syndrome.

Ma MH, Chen SY, Chiang WC, Su CP, Chen WJ.

Publication Types:

Comment

Letter

PMID: 15684216 [PubMed - indexed for MEDLINE]

3: Annu Rev Med. 2005 Feb 18;56:357-381.

SEVERE ACUTE RESPIRATORY SYNDROME (SARS): A Year in Review.

Skowronski DM, Astell C, Brunham RC, Low DE, Petric M, Roper RL, Talbot PJ, Tam T, Babiuk L.

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Severe acute respiratory syndrome (SARS) emerged from China as an untreatable and rapidly spreading respiratory illness of unknown etiology. Following point source exposure in February 2003, more than a dozen guests infected at a Hong Kong hotel seeded multi-country outbreaks that persisted through the spring of 2003. The World Health Organization responded by invoking traditional public health measures and advanced technologies to control the illness and contain the cause. A novel coronavirus was implicated and its entire genome was sequenced by mid-April 2003. The urgency of responding to this threat focused scientific endeavor and stimulated global collaboration. Through real-time application of accumulating knowledge, the world proved capable of arresting the first pandemic threat of the twenty-first century, despite early respiratory-borne spread and global susceptibility. This review synthesizes lessons learned from this remarkable achievement. These lessons can be applied to re-emergence of SARS or to the next pandemic threat to arise.

PMID: 15660517 [PubMed - as supplied by publisher]

4: Can J Public Health. 2005 Jan-Feb;96(1):52-4.

The financial impact of controlling a respiratory virus outbreak in a teaching hospital: lessons learned from SARS.

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**BACKGROUND:** Outbreaks of Severe Acute Respiratory Syndrome (SARS) in 2003 and renewed concerns regarding pandemic influenza have resulted in widespread planning for future respiratory disease outbreaks. Such planning should include accurate cost estimates for any proposed disease control strategies. From the acute care hospital perspective, such estimates typically take into account the cost of supplies and equipment, but rarely consider indirect costs such as lost revenue due to the scaling down of programs. **METHODS:** Retrospective cost analysis. Costs and savings were calculated from the hospital perspective using financial records. Costs were categorized to determine the major areas of expenditure and savings. **RESULTS:** We report that controlling a SARS outbreak in a teaching hospital over an 8-week period cost dollar12 million Canadian. Lost revenue and labour accounted for two thirds of the costs incurred while excess spending on services, materials, supplies and renovation of existing space accounted for the remaining one third. **CONCLUSIONS:** Cost estimates that consider only excess expenditures may considerably underestimate the true cost of infection control strategies.

PMID: 15682697 [PubMed - in process]

5: Clin Infect Dis. 2005 Feb 15;40(4):633-4; author reply 634-5.

Outbreak of methicillin-resistant *Staphylococcus aureus* infection associated with an outbreak of severe acute respiratory syndrome.

Bassetti S, Bischoff WE, Sherertz RJ.

Publication Types:

Comment  
Letter

PMID: 15712093 [PubMed - in process]

6: Clin Infect Dis. 2005 Feb 15;40(4):632-3.

Paradoxical increase in methicillin-resistant *Staphylococcus aureus* acquisition rates despite barrier precautions and increased hand washing compliance during an outbreak of severe acute respiratory syndrome.

Chai LY, Ng TM, Habib AG, Singh K, Kumarasinghe G, Tambyah PA.

Publication Types:

Comment  
Letter

PMID: 15712092 [PubMed - in process]

7: Clin Lab Haematol. 2005 Feb;27(1):15-20.

Haematological parameters in severe acute respiratory syndrome.

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Summary Clinical presentation of severe acute respiratory syndrome (SARS) is non-specific and isolation of all suspected patients is difficult because of the limited availability of isolation facilities. We studied changes in haematological parameters in SARS patients using median values analysed according to the day of symptom onset. White cell (WCC), absolute neutrophil, absolute lymphocyte (ALC) and platelet counts followed a v-shaped trend with the nadir at day 6 or 7 after symptom onset except for ALC in the ICU group that had not reached the nadir by day 12. None of our patients had a platelet count  $< 80 \times 10^9/l$  and WCC  $< 2 \times 10^9/l$  in the first 5 days of symptoms and these parameters may allow early stratification of febrile patients into likely and unlikely SARS cases to allow effective utilization of isolation facilities. On multivariate analysis, age is the only independent predictor for ICU admission.

PMID: 15686503 [PubMed - in process]

8: Curr Opin Crit Care. 2005 Feb;11(1):77-81.

Noninvasive ventilation for acute respiratory failure.

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**PURPOSE OF REVIEW:** This review critically examines recent literature related to applications of noninvasive ventilation in the acute setting. **RECENT FINDINGS:** Recent articles have strengthened the evidence supporting the use of noninvasive ventilation for patients with cardiogenic pulmonary edema and exacerbation of severe chronic pulmonary obstructive disease. In the former, however, it remains unclear whether noninvasive ventilation offers any significant advantages over continuous positive airway pressure. The rate of myocardial infarction seems to be no higher when patients with cardiogenic pulmonary edema are treated with noninvasive ventilation rather than continuous positive airway pressure, although caution is still advised in patients with acute coronary syndromes. Noninvasive ventilation also does not seem to increase the risk of dissemination of severe acute respiratory syndrome to health care workers as long as strict isolation procedures are used. Noninvasive ventilation facilitates weaning in patients with chronic obstructive pulmonary disease but should not be used routinely to treat extubation failure, and necessary intubation should not be delayed. Guidelines for the use of noninvasive ventilation can alter caregivers' behavior but have not been clearly shown to improve outcomes. Outcomes do seem to improve, however, as caregivers acquire experience with the technique. **SUMMARY:** The recent literature has refined some of the current indications for noninvasive ventilation in the acute-care setting, including chronic pulmonary obstructive disease and cardiogenic pulmonary edema. Guidelines for use are now being developed, and outcomes seem to be improving, partly as a consequence of greater caregiver experience and possibly related to technologic advances.

PMID: 15659949 [PubMed - in process]

9: Emerg Infect Dis. 2005 Jan;11(1):135-8.

SARS clinical features, United States, 2003.

Srikantiah P, Charles MD, Reagan S, Clark TA, Pletz MW, Patel PR, Hoekstra RM, Lingappa J, Jernigan JA, Fischer M.

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We compared the clinical features of 8 U.S. case-patients with laboratory-confirmed severe acute respiratory syndrome (SARS) to 65 controls who tested negative for SARS coronavirus (SARS-CoV) infection. Shortness of breath, vomiting, diarrhea, progressive bilateral infiltrates on chest radiograph, and need for supplemental oxygen were significantly associated with confirmed SARS-CoV infection.

PMID: 15705339 [PubMed - in process]

10: Emerg Infect Dis. 2004 Dec;10(12):2200-3.

SARS molecular detection external quality assurance.

Drosten C, Doerr HW, Lim W, Stohr K, Niedrig M.

Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany.

Inactivated severe acute respiratory syndrome-associated coronavirus samples were used for an external quality assurance study within the World Health Organization SARS Reference and Verification Network and other reference institutions. Of 58 participants, 51 correctly detected virus in all samples  $\geq 9,400$  RNA copies per milliliter and none in negative samples. Commercial test kits significantly improved the outcome.

PMID: 15663861 [PubMed - in process]

11: Eur J Emerg Med. 2005 Feb;12(1):13-18.

The psychological impact of severe acute respiratory syndrome outbreak on healthcare workers in emergency departments and how they cope.

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**OBJECTIVES:** The objectives of the present study were to examine the degree and the sources of mental distress and the coping strategies adopted by healthcare workers (HCW) of emergency departments (ED) in Hong Kong during the outbreak of severe acute respiratory syndrome (SARS). **METHODS:** Questionnaires were sent to

all doctors, nurses and healthcare assistants (HCA) working in the ED of all public hospitals. The overall degree of mental distress was measured by a single-item 11-point Likert scale. The source of distress was measured by an 18-item questionnaire, which was designed based on the experience of clinical psychologist colleagues providing counselling to staff taking care of SARS patients. The Brief Cope questionnaire was used to study coping strategies adopted by staff. RESULTS:: A total of 1260 questionnaires were sent out and the response rate was approximately 37%. The mean overall distress level was 6.19 out of a 10-point scale. The mean overall distress levels for doctors, nurses and HCA were 5.91, 6.52 and 5.44, respectively ( $F(2,420)=6.47$ ,  $P<0.005$ ). The overall distress level for nurses was significantly higher than for HCA ( $P<0.005$ ) but not doctors. The overall distress level was highly and significantly correlated with the six sources of distress: vulnerability/loss of control ( $r=0.68$ ); health of self ( $r=0.62$ ); spread of virus ( $r=0.60$ ); health of family and others ( $r=0.59$ ); changes in work ( $r=0.46$ ); being isolated ( $r=0.45$ ). The scores for nurses were significantly higher than for doctors in terms of the six sources of distress (all  $P$  values  $<0.01$ ). HCA were significantly higher than doctors (but not nurses) in worrying about their family's and others' health ( $P<0.05$ ). In terms of coping strategies, doctors were significantly more likely than nurses and HCA to use planning ( $P<0.05$  and  $<0.01$  respectively); nurses were significantly more likely than doctors to use behavioural disengagement ( $P<0.01$ ); whereas HCA were significantly more likely than doctors to use self distractions ( $P<0.05$ ). CONCLUSIONS:: SARS had caused a significant level of distress among ED staff. The distress level was highest for nurses, followed by doctors and HCA. The three most important variables that could account for the distress level were loss of control/vulnerability, fear for self-health and spread of the virus. Overall, the more frequently adopted coping strategies were acceptance, active coping, and positive framing.

PMID: 15674079 [PubMed - as supplied by publisher]

12: Int J Infect Dis. 2005 Mar;9(2):77-85.

SARS in Taiwan: an overview and lessons learned.

Chen KT, Twu SJ, Chang HL, Wu YC, Chen CT, Lin TH, Olsen SJ, Dowell SF, Su IJ; Taiwan SARS Response Team.

Field Epidemiology Training Program, Department of Health, Center for Diseases Control, Taiwan; Taipei City STD Control Center, Department of Health, Taipei City, Taiwan.

OBJECTIVES:: This report aims to describe the epidemiology of severe acute respiratory syndrome (SARS) in Taiwan between March and July 2003, and to examine the public health response. METHODS:: Surveillance for SARS was initiated on 14 March 2003. Response activities are described for the isolation of patients; contact tracing; quarantine of contact persons; fever screening for inbound and outbound passengers at the airport; and hospital infection control as assessed by mobile SARS containment teams. RESULTS:: Between 14 March and 30 July 2003 a total of 668 probable cases of SARS were reported. Of the 668 cases, 181 (27%) were fatal. Compared to the survivors, fatal cases were more likely to be older ( $p<0.001$ ), male ( $p<0.05$ ), exposed through hospital contact ( $p<0.001$ ), and have a coexisting medical disorder ( $p<0.001$ ). Between 28 March and 30 July a total of 151,270 persons were quarantined. Among them, 46 (3.0/10,000) were subsequently classified as being probable SARS cases. At the time of the mobile

team assessments, 46 (53%) hospitals had implemented WHO infection control recommendations. CONCLUSIONS:: In this outbreak, an emergency plan consisted of patient isolation and strict hospital infection control.

PMID: 15708322 [PubMed - in process]

13: Int J Occup Environ Health. 2004 Oct-Dec;10(4):421-7.

Severe acute respiratory syndrome (SARS) and healthcare workers.

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The recent outbreak of severe acute respiratory syndrome (SARS) was spread by international air travel, a direct result of globalization. The disease is caused by a novel coronavirus, transmitted from human to human by droplets or by direct contact. Healthcare workers (HCWs) were at high risk and accounted for a fifth of all cases globally. Risk factors for infection in HCWs included lack of awareness and preparedness when the disease first struck, poor institutional infection control measures, lack of training in infection control procedures, poor compliance with the use of personal protection equipment (PPE), exposure to high-risk procedures such as intubation and nebulization, and exposure to unsuspected SARS patients. Measures to prevent nosocomial infection included establishing isolation wards for triage, SARS patients, and step-down; training and monitoring hospital staff in infection-control procedures; active and passive screening of HCWs; enforcement of droplet and contact precautions; and compliance with the use of PPE.

PMID: 15702757 [PubMed - in process]

14: J Altern Complement Med. 2004 Dec;10(6):1041-51.

Chinese herbal medicine for severe acute respiratory syndrome: a systematic review and meta-analysis.

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Objectives: To review randomized controlled trials (RCTs) evaluating the effects of Chinese herbal medicine for treating severe acute respiratory syndrome (SARS) systematically. Design: Electronic and manual searches identified RCTs comparing Chinese medicine integrated to conventional medicine versus conventional medicine alone. Methodological quality of trials was assessed by generation of allocation sequence, allocation concealment, blinding, and intention-to-treat. Results: Eight RCTs (488 patients with SARS) were included. The methodological quality was generally low. The combined therapy showed significant reduction of mortality (relative risk 0.32 [95% confidence interval {CI} 0.12 to 0.91]), shortened duration of fever, symptom relief, reductions in chest radiograph abnormalities, and reductions in secondary fungal infections among patients receiving glucocorticoids. There were no significant effects on quality of life or glucocorticoid dosage.

Conclusion: Chinese herbal medicine combined with conventional medicine may have beneficial effects in patients with SARS. The evidence is insufficient because of the low methodological quality of the included trials.

PMID: 15674000 [PubMed - in process]

15: J Clin Microbiol. 2005 Feb; 43(2):962-5.

Detection of Severe Acute Respiratory Syndrome Coronavirus RNA in Plasma during the Course of Infection.

Wang WK, Fang CT, Chen HL, Yang CF, Chen YC, Chen ML, Chen SY, Yang JY, Lin JH, Yang PC, Chang SC.

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We examined severe acute respiratory syndrome-associated coronavirus (SARS-CoV) RNA in plasma of 32 patients (probable SARS cases) by a quantitative real-time reverse transcription-PCR assay and reported that the highest detection rate, 75%, was found between day 5 and day 7 of illness, followed by rates of 64, 50, and 38% found between day 8 and day 11, day 2 and day 4, and day 12 and day 16, respectively. Analysis of sequential SARS-CoV load in plasma from six cases revealed different patterns of viremia, with the peak between day 4 and day 8. Our findings of the high detection rate of SARS-CoV RNA in plasma before day 11, together with the relative convenience of collecting and handling plasma, suggest that plasma can be used for early diagnosis of SARS.

PMID: 15695719 [PubMed - in process]

16: J Clin Nurs. 2005 Jan; 14(1):28-34.

SARS (Severe Acute Respiratory Syndrome): reflective practice of a nurse manager.

Lau PY, Chan CW.

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**Aims and objectives.** This paper describes the reflective practice of a nurse manager in Hong Kong in supporting frontline nurses to overcome the crisis of SARS.  
**Background.** SARS infection was a crisis for everyone in endemic areas because of its threat to physical and emotional health. Hong Kong was the second leading endemic area in the world. Inadequate supplies of protective devices and the death of a nurse infected with SARS triggered nurses' negative emotions.  
**Methods.** A model of structured reflection was adopted to examine one's practice. A problem-solving model for crisis intervention was integrated into the reflective stage of structured reflection.  
**Results.** Promotion of nurses' safety and emotional stability were the major goals in handling the crisis. Strategies were employed including self-awareness, empowerment and team building, information sharing, provision of personal protective equipment and emotional support for frontline nurses.  
**Conclusions.** SARS infection threatens the physical and emotional health of nurses. From a positive perspective, such a crisis created an opportunity to learn and grow in



terms of ethical, personal and aesthetic arenas. Relevance to clinical practice. SARS epidemic raised worldwide attention and challenged the Hong Kong's health care system. Reflective practice is useful to guide and examine nurses' professional action during the crisis, and to put the experience into a learning perspective.

PMID: 15656845 [PubMed - in process]

17: J Emerg Med. 2005 Feb;28(2):225-6.

SARS and the Hospital Emergency Incident Command System (HEICS): Outbreak management as the mother of invention.

Jacoby IJ.

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Publication Types:  
Editorial

PMID: 15707823 [PubMed - in process]

18: J Emerg Med. 2005 Feb;28(2):185-96.

Implementation of the Hospital Emergency Incident Command System during an outbreak of severe acute respiratory syndrome (SARS) at a hospital in Taiwan, ROC.

Tsai MC, Arnold JL, Chuang CC, Chi CH, Liu CC, Yang YJ.

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We sought to describe the implementation of the Hospital Emergency Incident Command System (HEICS) at National Cheng Kung University Hospital (NCKUH) in Taiwan, ROC during the outbreak of severe acute respiratory syndrome (SARS) in early 2003. We administered a 14-question survey via structured interviews to individuals occupying activated HEICS leadership positions at NCKUH to identify the organization, structure, and function of the HEICS units and subunits they led and the job actions they performed from 25 March to 16 June 2003. Thirty-three of 38 persons (87%) occupying 39 of 44 (89%) activated HEICS leadership positions directly participated in the survey. The participants collectively reported: 1) the creation of four new HEICS unit leader positions and corresponding units during the outbreak, including the infection control officer (administrative section) and SARS assessment, isolation, and critical care unit leaders (operations section); 2) the creation of six new HEICS subunits, including functional areas for fever screening, SARS assessment, and resuscitation outside the hospital, and SARS patient care, SARS critical care, and employee isolation inside the hospital; and 3) the performance of new job actions related to infection control by all HEICS unit leaders. HEICS provides a flexible framework that seems to have assisted NCKUH in the organization of its emergency response to the SARS outbreak in Taiwan, ROC.

PMID: 15707815 [PubMed - in process]

19: J Immunol Methods. 2005 Jan;296(1-2):37-44. Epub 2004 Dec 10.

Evaluation of a safe and sensitive Spike protein-based immunofluorescence assay for the detection of antibody responses to SARS-CoV.

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Previously, we have identified a truncated antigenic fragment named protein C [441 to 700 amino acids (a.a.)] as the immunodominant fragment of Spike (S) protein of severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV). We have now successfully expressed protein C using the baculovirus system in *S. frugiperda* (Sf-9) cells. This recombinant baculovirus expressing protein C was first characterized using five SARS convalescent human sera and five normal human sera. The results showed that protein C is an authentic antigen against SARS-CoV antibody. Our Spike protein-based immunofluorescence assay (IFA) based on this recombinant baculovirus-Sf-9 system was further assessed with a panel of 163 clinical samples collected during the SARS epidemic in Singapore, which include samples from 21 clinically confirmed SARS, 42 non-SARS patient sera, and 100 normal sera. The results were compared to a commercial SARS IFA kit (EUROIMMUN, Germany) and a conventional IFA test performed in Singapore General Hospital. All of the 21 SARS-positive serum samples could be recognized by our IFA, giving a specificity and sensitivity of 100%, which was compatible with both whole virus-based IFA assays. No cross-reactivity with serum samples against infectious bronchitis virus (IBV) and transmissible gastroenteritis virus (TGEV) were detected in our assays. Thus, our Spike protein-based IFA could offer a safer procedure which can be performed in a BSL-2 laboratory as it could mimic the whole virus based-IFA without any loss of sensitivity and specificity. It is also more user-friendly and cost-effective than the whole virus-based IFA.

PMID: 15680149 [PubMed - in process]

20: Med Care. 2005 Feb;43(2):168-72.

The impact of the SARS outbreak on an urban emergency department in Taiwan.

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**OBJECTIVE:** Emergency departments (ED) were on the front lines for possible cases of transmission during the severe acute respiratory syndrome (SARS) epidemic. The purpose of this study was to investigate the impact of the SARS catastrophe on an urban ED. **METHODS:** The patients' characteristics in an urban ED were collected from March to May 2003 during the SARS outbreak in Taiwan. The crisis period was divided into 2 periods: 30 days before (period 1) and after (period 2) April 21, the date of the first hospital-associated transmission. Problem severity in the ED and stress levels of ED staff during the SARS catastrophe were rated from mild (1 point) to severe (5 points). **RESULTS:** The number of ED patients declined 33.4% in period 2. There was a 2.1% (95%CI, 0.4-3.8) increase in the percentage of male patients, a 2.5% (95% CI, 1.5-3.7) increase in percentage of fever (>38 degrees C), and a 4.0% (95% CI, 2.6-5.4%) increase in chief complaint of fever in period 2. The

number of nontrauma patients younger than 18 years had declined by 44.5% in period 2. The total charge for reimbursement from an insurance institution declined 21.7%. During the SARS outbreak, the most severe stress experienced by either physicians or nurses occurred during emergency resuscitation (median stress rating point, 4; interquartile range, 1). CONCLUSION: The SARS catastrophe affected the ED visit volume, finances, various patient characteristics, and stress levels in the ED physicians and nurses. EDs must be fully prepared to face the challenges of the next outbreak of SARS or other infectious disease.

PMID: 15655430 [PubMed - in process]

21: Psychol Med. 2004 Oct;34(7):1197-204.

Severe acute respiratory syndrome (SARS) in Hong Kong in 2003: stress and psychological impact among frontline healthcare workers.

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BACKGROUND: The outbreak of severe acute respiratory syndrome (SARS) posed an unprecedented threat and a great challenge to health professionals in Hong Kong. The study reported here aimed at investigating the origin of stress and psychological morbidity among frontline healthcare workers in response to this catastrophe.

METHOD: Self-administered questionnaires were sent to frontline healthcare workers in three hospitals. The General Health Questionnaire was used to identify psychological distress. Socio-demographic and stress variables were entered into a logistic regression analysis to find out the variables associated with psychological morbidity. RESULTS: The response rate was 40 %. Sixty-eight per cent of participants reported a high level of stress. About 57 % were found to have experienced psychological distress. The healthcare workers' psychological morbidity was best understood by the perceptions of personal vulnerability, stress and support in the workplace. CONCLUSION: These findings shed light on the need for hospital administrators to be aware of the extent and sources of stress and psychological distress among frontline healthcare workers during disease outbreak.

PMID: 15697046 [PubMed - in process]

22: Psychol Med. 2004 Oct;34(7):1187-95.

Psychological distress and negative appraisals in survivors of severe acute respiratory syndrome (SARS).

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BACKGROUND: Severe acute respiratory syndrome (SARS) is a novel disease. The authors have limited knowledge of its impact on mental health. The present study aimed to examine the level and extent of psychological distress of SARS survivors following 1-month recovery, to explore patients' negative appraisals of the impact of

SARS, and to evaluate the associations between psychological distress and negative appraisals. METHOD: The Beck Anxiety Inventory, the Beck Depression Inventory, and a newly developed measure, the SARS Impact Scale (SIS), were mailed to 453 Hong Kong Chinese SARS survivors discharged from hospital for 4 weeks or more. RESULTS: A total of 425 patients received the questionnaires and 180 (mean age 36.9 years; 120 women) gave valid replies. The response rate was 42.4 %. The participants also represented 13.6 % of all adult survivors in Hong Kong. About 35 % of respondents reported 'moderate to severe' or 'severe' ranges of anxiety and/or depressive symptoms. It was found that those working as healthcare workers or having family members killed by SARS were more prone to develop subsequent high levels of distress. Factor analyses extracted three meaningful factors of the SIS, namely 'survival threat', 'physical impact', and 'social impact'. Negative appraisals at the acute phase and 1-month recovery significantly accounted for substantial portions of variances for anxiety and depressive symptoms, after the effects of other psychosocial variables were controlled. CONCLUSIONS: Psychological distress of SARS survivors at 1-month recovery is real and significant. Negative appraisals may play a pivotal role in the development of psychological distress for SARS survivors, at least in the short term.

PMID: 15697045 [PubMed - in process]

23: Rev Sci Tech. 2004 Aug;23(2):443-51.

Factors and determinants of disease emergence.

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Emerging infectious diseases can be defined as infections that have newly appeared in a population or are rapidly increasing in incidence or geographic range. Many of these diseases are zoonoses, including such recent examples as avian influenza, severe acute respiratory syndrome, haemolytic uraemic syndrome (a food-borne infection caused by certain strains of *Escherichia coli*) and probably human immunodeficiency virus/acquired immune deficiency syndrome. Specific factors precipitating the emergence of a disease can often be identified. These include ecological, environmental or demographic factors that place people in increased contact with the natural host for a previously unfamiliar zoonotic agent or that promote the spread of the pathogen. These factors are becoming increasingly prevalent, suggesting that infections will continue to emerge and probably increase. Strategies for dealing with the problem include focusing special attention on situations that promote disease emergence, especially those in which animals and humans come into contact, and implementing effective disease surveillance and control.

PMID: 15702712 [PubMed - in process]

24: Viral Immunol. 2004;17(4):535-44.

Severe acute respiratory syndrome, a pathological immune response to the new coronavirus--implications for understanding of pathogenesis, therapy, design of vaccines, and epidemiology.

Bermejo JF, Munoz-Fernandez MA.

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Findings coming from autopsies and serum of SARS patients suggest an important immune-inflammatory implication in the evolution to respiratory distress. Conditions such as HIV infection or treatment with immunosuppressors (in cancer or autoimmune diseases) are not among the bad prognosis factors for development of distress. To date, there have been no reported case fatalities in children, probably due to their more immature immune system. Our conclusions follow: (1) The milder form of SARS in children and the apparent protective factor that immunosuppression represent rules out a significant viral cytopathic effect (they would be the most affected). (2) The evidence for immune implication in distress strongly supports immunomodulators for therapy: phosphodiesterase inhibitors (due to their down-modulating activity on proinflammatory cytokines); inhaled corticoids (aimed at producing a local immunomodulation); teophylline or nedocromil sodium (which prevents inflammatory cell recruitment into the airway wall). (3) An early immunomodulatory therapy, based on the levels of proinflammatory cytokines and clinical parameters to evaluate the respiratory function such as arterial oxygen saturation, could prevent the occurrence of distress. (4) Vaccine design should consider the immune origin of distress. (5) Physicians should be aware of mildly symptomatic patients (children, immuno-compromised hosts) to avoid transmission to immunocompetent adults.

PMID: 15671750 [PubMed - in process]

25: *Viral Immunol.* 2004;17(4):528-34.

Structure-based preliminary analysis of immunity and virulence of SARS coronavirus.

Li Y, Luo C, Li W, Xu Z, Zeng C, Bi S, Yu J, Wu J, Yang H.

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The research on SARS-associated coronavirus (SARS-CoV) has not stopped since its discovery, but the pathogenesis of SARS is still unclear. To explore the possible molecular mechanisms of the invasion and virulence of SARS-CoV, we investigated the structural basis of the viral proteins using computational biology. Forty-five motifs relating to superantigens, toxins and other bioactive molecules were detected in the proteins of SARS-CoV. The results showed that the distribution of the motifs varied in different proteins. Enzyme-like motifs were located in the R protein, while ICAM-1-like and toxin-like molecules were located in the spike, envelop, nucleocapsid, PUP1, PUP 2 and PUP 4 proteins. Comparison of SARS-CoV with other viruses (OC43, PEDV, HRSV, HHV and HAdenoV) showed that each group of motifs was different for each type of virus. Data suggest that the proteins of SARS-CoV with toxic motifs might play crucial roles in targeting host cells and interfering

with the immune system. This study provides new information for drug and vaccine design, as well as therapeutic strategies against SARS.

PMID: 15671749 [PubMed - in process]

26: Virol J. 2005 Feb 10;2(1):7 [Epub ahead of print]

Reference gene selection for quantitative real-time PCR analysis in virus infected cells: SARS corona virus, Yellow fever virus, Human Herpesvirus-6, Camelpox virus and Cytomegalovirus infections.

Radonic A, Thulke S, Bae HG, Muller MA, Siegert W, Nitsche A.

Ten potential reference genes were compared for their use in experiments investigating cellular mRNA expression of virus infected cells. Human cell lines were infected with Cytomegalovirus, Human Herpesvirus-6, Camelpox virus, SARS coronavirus or Yellow fever virus. The expression levels of these genes and the viral replication were determined by real-time PCR. Genes were ranked by the BestKeeper tool, the GeNorm tool and by criteria we reported previously. Ranking lists of the genes tested were tool dependent. However, over all, beta-actin is an unsuitable as reference gene, whereas TATA-Box binding protein and peptidyl-prolyl-isomerase A are stable reference genes for expression studies in virus infected cells.

PMID: 15705200 [PubMed - as supplied by publisher]